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Supplemental References

Cohort descriptions

Cardiovascular Health Study (CHS)

The CHS is a population-based cohort study of risk factors for CHD and stroke in adults ≥65 years conducted across four field centers in the United States. [The original predominantly European-ancestry cohort of 5201 persons was recruited in 1989-1990 from a random sample of people on Medicare eligibility lists and an additional 687 African-Americans were enrolled subsequently for a total sample of 5888. Blood samples were drawn from all participants at their baseline examination and DNA was subsequently extracted from available samples. Genotyping was performed at the General Clinical Research Center's Phenotyping/Genotyping Laboratory at Cedars-Sinai among CHS participants who consented to genetic testing and had DNA available using the Illumina HumanExome v.1.0 BeadChip array. Genotypes were jointly called at The University of Texas Health Science Center at Houston as part of approximately 62,000 ethnically-diverse samples from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium.[1] Analyses were performed separately for individuals of European and African ancestries.

Diabetes Heart Study (DHS)

The Diabetes Heart Study (DHS) is a family-based observational cohort study of cardiovascular disease from a single research center in the United States.[2] The original predominantly (85%) European-ancestry cohort of 1443 persons was recruited in 1997-2005 from a random from families with at least two type 2 diabetes affected siblings and, if possible, a non-diabetic sibling. Blood samples were drawn from all participants at their baseline examination and DNA was subsequently extracted from available samples. Genotyping was performed on the Illumina HumanExome v.1.0 BeadChip array at the Center for Genomics and Personalized Medicine Research at Wake Forest University School of Medicine. Genotypes were called using ZCall[3] and QC was performed at Wake Forest University Center for Genomics and Personalized Medicine Research.

Jackson Heart Study (JHS)

The JHS aimed at enrolling representative, population-based cohort of self-defined African-American persons aged 35–84 years, with an embedded collection of families for genetic study.[4] Participants were enrolled from the three counties that make up the Jackson, Mississippi metropolitan area. Relatives of selected participants were recruited to develop a large, nested family cohort. Participants provided extensive medical and social history, had an array of physical and biochemical measurements and diagnostic procedures, and provided genomic DNA. Data and biologic materials have been collected from 5302 adult African Americans, including 1499 members of 291 families. Participants have a high prevalence of diabetes, hypertension, obesity, and related disorders. Genotyping was performed among JHS participants who consented to genetic testing and had DNA available using the Illumina HumanExome v.1.0 BeadChip array. Genotypes were jointly called at The University of Texas Health Science Center at Houston as part of approximately 62,000 ethnically-diverse samples from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium.[1] Individuals that overlapped with ARIC were removed.

Family Heart Study (FamHS)

The FamHS (https://dsgweb.wustl.edu/fhscc/) began in 1992 with the ascertainment of 1,200 families, half randomly sampled and half selected because of an excess of CHD or risk factor abnormalities as compared with age- and sex-specific population rates.[5] The families, with approximately 6,000 subjects, were sampled from four population-based parent studies: the Framingham Heart Study, the Utah Family Tree Study, and two centers for the Atherosclerosis Risk in Communities study (ARIC: Minneapolis, and Forsyth County, NC). These individuals attended a clinic visit between the years 1994-1996 and a broad range of phenotypes were assessed in the general domains of CHD, atherosclerosis, cardiac and vascular function, inflammation and hemostasis, lipids and lipoproteins, blood pressure, diabetes and insulin resistance, pulmonary function, diet, habitual physical activity, anthropometry, medical history and medication use. Approximately 8 years later, study participants belonging to the largest pedigrees were invited for a second clinical exam (2002-04) and computed tomography scan measurements were assessed, among many other phenotypes. A total of 2,756 European American (EA) subjects in 510 extended random and high CHD risk families were studied. A total of 1,865 key EA subjects within this group of families were genotyped using the Illumina Infinium HumanExome v1.0 BeadChip. In addition, 633 African American (AA) subjects were recruited at an additional ARIC field center at the University of Alabama in Birmingham. A total of 608 AA subjects were genotyped using the Illumina Infinium HumanExome v1.0 BeadChip. Informed consent was obtained from all participants, and this project was approved by the Institutional Review Boards of all participating institutions.

Lothian Birth Cohort 1936 (LBC1936)

The LBC1936 consists of 1,091 relatively healthy individuals assessed on cognitive and medical traits at about 70 years of age. They were all born in 1936 and most took part in the Scottish Mental Survey of 1947. At baseline the sample of 548 men and 543 women had a mean age 69.6 years (SD = 0.8). They were all Caucasian, community-dwelling, and almost all lived in the Lothian region (Edinburgh city and surrounding area) of Scotland. A full description of participant recruitment and testing can be found elsewhere.[6] 988 individuals were genotyped using the Illumina HumanExome BeadChip at the Wellcome Trust Clinical Research Facility, Edinburgh.

SHIP / SHIP-Trend

SHIP is a population-based project in West Pomerania, a region in the northeast of Germany, that consists of two independent prospectively collected cohorts (SHIP and SHIP-TREND) assessing the prevalence and incidence of common population-based diseases and their risk factors. The study design has been previously described in detail.[7] Briefly, a sample from the population aged 20 to 79 years was drawn from population registries. First, the three cities of the region (with 17,076 to 65,977 inhabitants) and the 12 towns (with 1,516 to 3,044 inhabitants) were selected, and then 17 out of 97 smaller towns (with less than 1,500 inhabitants), were drawn at random. Second, from each of the selected communities, subjects were drawn at random, proportional to the population size of each community and stratified by age and gender. Only individuals with German citizenship and main residency in the study area were included. For SHIP, baseline examinations were carried out from 1997 until 2001, and the sample finally comprised 4,308 participants. Baseline examinations for SHIP-TREND were carried out between 2008 and 2012, finally comprising 4420 participants. Analyses were performed separately for individuals of both cohorts.

Genetic Study of Atherosclerosis Risk (GeneSTAR)
GeneSTAR is a family-based prospective study of risk factors, occult disease, and incident cardiovascular disease in siblings, later extended to offspring and whole pedigrees. European- and African American families were identified from probands with early-onset (< age 60) coronary artery disease (CAD) hospitalized in any of 10 Baltimore hospitals between 1983 and 2007. Siblings completed baseline screening between 1983 and 2007, while offspring, co-parents of the offspring, and additional siblings completed baseline screening between 2003 and 2007. Siblings were followed every 5 years for cardiovascular and other comorbid incident events. DNA was collected at baseline (1991-2007) or follow-up (for those whose baseline visit was pre-1991). Probands were not eligible if they had CAD associated with calcific aortic stenosis or chronic glucocorticosteroid therapy, following organ transplantation or post intensive chest radiation, had an autoimmune diseases like systemic lupus, or if they had a cocaine-induced myocardial infarction. Participants younger than age 21 or older than age 80, who had known CAD or an autoimmune disease such as systemic lupus, were taking chronic glucocorticosteroids, had undergone any organ transplantation, or had major comorbidity that had a life expectancy under 5 years of age were excluded. The full sample includes 4423 participants, 51% female/49% male, and 38% African American/61% European American/1% other American. Genotyping was performed by the Northwest Genomics Center at the University of Washington through the RS&G service using the Illumina HumanExome v.1.2 BeadChip array. Analyses were performed separately for European and African Americans.

ImaGene
Project 'Cardiovascular phenotype-genotype analysis with a CT based lung cancer screening trial' within the Population Imaging Genetics (ImaGene) study was set up to investigate the relationship between genetics and image characteristics related to cardiovascular disease in an at-risk population of current or former heavy smokers between 50 and 75 years of age. 905 participants of the Dutch-Belgian lung cancer screening trial (NELSON) were succesfully genotyped using the Illumina HumanExome v1.1 BeadChip array. Low-dose, non-ECG synchronized, non-contrast enhanced baseline chest CTs from the NELSON study were available for all participants. CTs were acquired on a 16 detector-row scanner (Mx8000 IDT, Somatom Sensation 16, or Brilliance 16P, Philips Medical Systems, Cleveland, OH, USA) in spiral mode with 16 × 0.75 mm collimation. Axial images of 1.0 mm thickness at 0.7 mm increment were reconstructed with a moderately soft kernel (Philips "B"). The peak voltage was 120–140 kVp depending on patient weight, with a tube current of 30 mAs.

Old Order Amish
The Amish Family Calcification Study (AFCS) was initiated in 2001 to identify the determinants of vascular calcification and to evaluate the relationship between calcification of bone and vascular tissue among members of the Old Order Amish community in Lancaster County.[8] For this study relatively healthy subjects and their family members were recruited from the Amish community between 2001 and 2006 for vascular imaging by electron beam CT scan. The final sample size comprised 1,075 subjects. Blood samples were drawn for biochemical assays and DNA analysis.

Framingham Heart Study (FHS)

Framingham Heart Study (FHS) is a community-based prospective study designed to investigate the incidence of cardiovascular diseases and factors related to its development. Study population was composed of three cohorts with European ancestry, original (5,209 participants ascertained systematically from two-thirds of the households in the town of Framingham, MA, beginning in 1948), Offspring (5,124 children of the original cohort, and spouses of those children, beginning in 1972), and the Third Generation (4,095 children of the Offspring cohort, beginning in 2002).[9, 10] In addition to the initial examination and face-to-face interview, participants were invited to follow-up examinations at the study clinics that were accomplished every two years for the original cohort or every four years for the Offspring and Gen3 cohorts. An un-related spouse cohort was formed in 2004 include 103 spouses of the offspring participants. Genotyping for more than 276,000 variants on the basis of the Illumina Infinium Human Exome Array v1.0 or v1.1 was conducted in 8351 FHS samples. Quality control of the genotye was accomplished through jointly called at The University of Texas Health Science Center at Houston as part of approximately 62,000 ethnically-diverse samples from the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium.[1]

BioImage – High Risk Plaque

The BioImage study (NCT00738725) is a multi-ethnic, observational study aimed at characterizing subclinical atherosclerosis in 6,699 US adults (55-80 years at baseline, 2008-2009) at risk for, but without, clinical ASCVD.[11] Participants were genotyped on the Illumina Infinium Human Exome Array v1.1.[12]

Multi-Ethnic Study of Atherosclerosis (MESA)

MESA is an NHLBI-sponsored population-based, prospective, multi-center cohort study including participants recruited from six field sites in the United States – Forsyth County, NC (Wake Forest University), Northern Manhattan/Bronx, NY (Columbia University), Baltimore/Baltimore County, MD (Johns Hopkins University), St. Paul, MN (University of Minnesota, Twin Cities), Chicago, IL (Northwestern University), and Los Angeles County, CA (UCLA). Details of recruitment and study design have been previously published elsewhere.[13] Briefly, the MESA cohort comprises 6,814 men and women of diverse ethnic background who were 45 to 84 years old at the baseline exam and free of clinically overt cardiovascular disease (CVD) who were recruited to elucidate the determinants and natural history of subclinical CVD, study progression of subclinical CVD, and its impact on incident clinical CVD. The cohort is 53% women with an ethnic composition of approximately 38% Caucasian, 28% African American, 22% Hispanic and 12% Asian, primarily of Chinese descent. Five clinical exams have taken place (2000-02, 2002-04, 2004-05, 2005-07, 2010-12), with follow-up every 9 to 12 months for events. The MESA was approved by the Institutional Review Board of all participating field sites and reading centers and participants gave informed consent for participation and use of DNA specimens. The current study includes data from African-Americans and Caucasians with available exome chip data, coronary artery calcium (CAC), and carotid intima media thickness (IMT) at the baseline exam (2000-02). Joint genotype calling for the exome chip V1.0 was performed at UT-Houston for all CHARGE samples, including for MESA. Additional QC was performed at Cedars-Sinai and University of Virginia. After QC, 238,895 SNPs remained for analysis.

Genetic Epidemiology Network of Arteriopathy (GENOA)

GENOA is one of four networks in the NHLBI Family-Blood Pressure Program (FBPP).[14] GENOA's long-term objective is to elucidate the genetics of target organ complications of hypertension, including both atherosclerotic and arteriolosclerotic complications involving the heart, brain, kidneys, and peripheral arteries. The longitudinal GENOA Study recruited European-American and African-American sibships with at least 2 individuals with clinically diagnosed essential hypertension before age 60 years. All other members of the sibship were invited to participate regardless of their hypertension status. Participants were diagnosed with hypertension if they had either 1) a previous clinical diagnosis of hypertension by a physician with current anti-hypertensive treatment, or 2) an average systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg based on the second and third readings at the time of their clinic visit. Exclusion criteria were secondary hypertension, alcoholism or drug abuse, pregnancy, insulin-dependent diabetes mellitus, or active malignancy. During the first exam (1995-2000), 1,583 European Americans from Rochester, MN and 1,854 African Americans from Jackson, MS were examined. Between 2000 and 2005, 1,241 of the European Americans returned for an examination that included a CT scan of the heart for coronary artery calcification. Between 2009 and 2011, 657 of the African Americans returned for an examination that included a CT scan of the heart for coronary artery calcification. Because African-American probands for GENOA were recruited through the Atherosclerosis Risk in Communities (ARIC) Jackson field center participants, we excluded ARIC participants from analyses. Written informed consent was obtained from all participants, and this project was approved by the Institutional Review Boards of all participating institutions. Both European Americans and African Americans were genotyped using the Illumina Infinium HumanExome v1.0 BeadChip. Genotyping and genotype calling for European Americans was performed at the University of Texas Health Sciences Center. Genotyping and genotype calling for African Americans was performed at the Center for Inherited Disease Research (CIDR).

AGES Reykjavik

The Reykjavik Study cohort originally comprised a random sample of 30,795 men and women born in 1907–1935 and living in Reykjavik in 1967. 2 A total of 19381 attended, resulting in 71% recruitment rate. The study sample was divided into six groups by birth year and birth date within month. One group was designated for longitudinal follow-up and was examined in all stages. One group was designated a control group and was not included in examinations until 1991. Other groups were invited to participate in specific stages of the study. Between 2002 and 2006, the AGES-Reykjavik study re-examined 5764 survivors of the original cohort who had participated before in the Reykjavik Study. The AGES Reykjavik Study GWAS was approved by the National Bioethics Committee (00-063- V8+1) and the Data Protection Authority. DNA was genotyped using the Illumina HumanExome v.1.0 BeadChip array. Samples were excluded from the dataset based on sample failure, genotype mismatch with reference panel, and sex mismatch, resulting in clean genotype data on 2,983 individuals. Standard protocols for working with Illumina data were followed, with clustering score greater than 0.4. SNPs were excluded using filters based on call rate (<97%), Hardy-Weinberg Equilibrium ($< 1\times10^{-6}$) 238,015 SNPs passing all QC (of 247,039 prior to cleaning steps).

Atherosclerosis Risk in Communities (ARIC)

ARIC is a population-based prospective study of men and women aged 45-64 years at baseline, which recruited 15,792 African American and White individuals from 4 U.S. communities to study the etiology and natural history of subclinical and clinical atherosclerosis. Participants were examined at baseline (1987-1989) and 4 follow-up clinic visits (1990-1992, 1993-1995, 1996-1998, 2011-2013), at which a rich array of health assessments have been made, with over 25 years of follow-up through annual phone updates for hospital admissions, medical history, and events.[15] DNA has been collected, with extensive genome-wide array and genetic sequencing data available.

Rotterdam Study (RS)
The Rotterdam Study (RS) is a prospective population-based cohort study among persons aged 55 years or older in the Ommoord district of Rotterdam, the Netherlands. The rationale and design of the Rotterdam Study have been described elsewhere.[16] The cohort started in 1990 and has been extended twice. The present sutdy used data for carotid intima media thickness from the baseline examination of the original cohort (RS-I, visit 1: 1990-1993) and for coronary calcification from the third examination of the original cohort (RS-I, visit 3: 1997-1999). The RS participants are interviewed and have an extensive set of examinations every 3-4 years and have been followed-up for a variety of diseases. The Rotterdam Study has been approved by the Medical Ethics Committee of the Erasmus MC and by the Ministry of Health, Welfare and Sport of the Netherlands , implementing the Wet Bevolkingsonderzoek: ERGO (Population Studies Act: Rotterdam Study). All participants provided written informed consent to participate in the study and to obtain information from their treating physicians. The approval has been renewed every 5 years, as well as with the introduction of major new elements in the study. The methods regarding the Exome Chip Array has been described in detial elsewhere.[1]

Erasmus Rucphen Family Study (ERF)
Erasmus Rucphen Family study (ERF) is a family based study conducted in a genetically isolated population in the South-West of the Netherlands, studied as part of the Genetic Research in Isolated Population (GRIP) program.[17, 18] The aim of this study is to identify genetic risk factors of complex diseases and genetic associations to complex traits. Study population includes aproximatelly 3,000 participants who are descendants of a limited number of founders living in the 19th century. All data were collected between 2002 and 2005. All participants gave written informed consent and the Medical Ethics Committee at Erasmus MC University Medical Center approved the study. Study participants from the ERF cohort (N = 1,527) were genotyped on the Illumina Infinium HumanExome BeadChip, version 1.1. Calling was performed with GenomeStudio and the ZCall variant calling tool (Broad Institute).[3]

Netherland Epidemiology of Obesity Study (NEO)
The NEO was designed for extensive phenotyping to investigate pathways that lead to obesity-related diseases. The NEO study is a population-based, prospective cohort study that includes 6,671 individuals aged between 45-65 years, with an oversampling of individuals with overweight or obesity. At baseline, information on demography, lifestyle, and medical history have been collected by questionnaires. In addition, samples of 24-h urine, fasting and postprandial blood plasma and serum, and DNA were collected. Genotyping was perfomed using the Ilumina HumanCoreExome chip, which was subsequently imputed to the 1000 genome reference panel. Participants underwent an extensive physical examination, including anthropometry, electrocardiography, spirometry, and measurement of the carotid artery intima-media thickness by ultrasonography. In random subsamples of participants, magnetic resonance imaging of abdominal fat, pulse wave velocity of the aorta, heart, and brain, magnetic resonance

spectroscopy of the liver, indirect calorimetry, dual energy X-ray absorptiometry, or accelerometry measurements were performed. The collection of data started in September 2008 and completed at the end of September 2012. Participants were currently being followed for the incidence of obesity-related diseases and mortality.[19]

Young Finns Study (YFS)

The Cardiovascular Risk in Young Finns Study (YFS) is a population-based follow up-study started in 1980. The main aim of the YFS is to determine the contribution made by childhood lifestyle, biological and psychological measures to the risk of cardiovascular diseases in adulthood. In 1980, over 3,500 children and adolescents all around Finland participated in the baseline study. The follow-up studies have been conducted mainly with 3-year intervals. The latest 30-year follow-up study was conducted in 2010-11 (ages 33-49 years) with 2,063 participants. The study was approved by the local ethics committees (University Hospitals of Helsinki, Turku, Tampere, Kuopio and Oulu) and was conducted following the guidelines of the Declaration of Helsinki. All participants gave their written informed consent.[20]

Genotyping methods

Genotypes from the Age, Gene/Environment, Susceptibility-Reykjavik (AGES) Study, Cardiovascular Health Study (CHS), Rotterdam Study (RS), Framingham Heart Study (FHS), Family Heart Study (FamHS), and Jackson Heart Study (JHS) were jointly called.[1] High Risk Plaque-Bioimage (Bioimage), genotyped with v1.1 of the Beadchip, was called in GenomeStudio (Illumina) using GenCall and low frequency variant calling was further refined using zCall.[3] The Diabetes Heart Study (DHS), Genetic Epidemiology Network of Arteriopathy Study (GENOA), ImaGene, Young Finns Study (YFS), Gene Study of Atherosclerosis Risk in Families (GeneSTAR), Old Order Amish Study (Amish), Netherlands Epidemiology of Obesity Study (NEO), Erasmus Ruchphen Family Study, Lothian Birth Cohort, Study of Health in Pomerania (SHIP), and SHIP-TREND were called in GenomeStudio (Illumina) using the joint calling cluster file and used zCall.

It is estimated that 95 % of European ancestry and 85% of African ancestry variation with minor allele frequency (MAF) > 0.1 % is captured by the content of the Illumina HumanExome Beadchip array.[21]

Variant quality control was performed jointly[1] and by individual cohorts. Low-performing variants from joint-calling were excluded from analysis.[1] 238,065 variants were included in analysis. Samples were excluded by each cohort if genotypes had poor concordance with prior genome-wide array-based genotypes when available, >5% of genotypes missing, they were population clustering outliers, had high inbreeding coefficients or heterozygosity rates, phenotypic and genotypic sex discordance, one from each duplicate (or monozygotic twin pairing), and high degrees of cryptic relatedness in studies without families was observed.[21] All variants were coded in an additive fashion. Variants were annotated using dbNSFP v2.0.[22]

Secondary Statistical Analyses

APOE ε2 Association Conditional on LDL cholesterol

To determine whether low-density lipoprotein (LDL) cholesterol is an important intermediary in the association between rs7412-T and CAC, we tested the association further adjusting for LDL cholesterol. In studies with available measures, fasting LDL cholesterol was obtained and/or calculated based on the Friedewald calculation when triglycerides were less than 400 mg/dL and directly measured when triglycerides were greater than 400 mg/dL. To account for the effect of lipid-lowering therapy, we adjusted LDL cholesterol to reflect the observation that statins, on average, reduce LDL cholesterol by 30% prior to conditioning.[23] Association analyses were performed within each cohort and meta-analyzed as described above with fasting LDL cholesterol as an additional covariate.

APOE ε2 Association Conditional on Other *APOE* Genotypes

The major *APOE* polymorphisms at 19q13.2 are ε2, ε3, and ε4.[24] The ε2 allele is determined by rs7412-T and the ε4 allele by rs429358-C, while the referent ε3 genotype has the rs7412-C / rs429358-T haplotype. Given the absence of rs429358 on the exome chip and prior genome-wide genotyping arrays, we obtained directly genotyped ε2, ε3, and ε4 by polymerase chain reaction in 5,872 participants from FHS, AGES, GENOA, CHS, and DHS. Our hypothesis was that the effect of the ε2 allele on subclinical atherosclerosis was independent of ε4 status. We tested the association of the *APOE* non-reference genotypes (ε3/ ε3 referent) with CAC stratified for ethnicity and sex while accounting for age and principal components within each cohort. We then performed a fixed-effects meta-analysis weighted by the inverse of variances to summarize the association across cohorts.

Association with CHD

To test for association of rs7412-T with prevalent CHD, we obtained summary results from an association analysis led by the Myocardial Infarction Genetics (MIGen) Consortium. 21,182 individuals of European ancestry, independent of the subclinical atherosclerosis analyses, were genotyped with the Illumina HumanExome Beadchip v1.0 at the Broad Institute (Cambridge, MA) and 9,472 of these individuals were classified as having CHD.[25] We obtained the single variant association results for rs7412-T accounting for age, sex, ethnicity, and principal components of ancestry.

We also determined the concordance of subclinical atherosclerosis genetic architecture with that of CHD. We focused on the concordance of effect direction of variants previously associated with CHD at a genome-wide level for individuals of European ancestry.[26] We selected the top associated CHD variant for each locus genotyped on the exome chip. Separately for CAC and CIMT, we determined the probability of a CHD variant having a concordant effect direction with each subclinical atherosclerotic trait. We determined the likelihood of effect observed concordance compared to chance accounting for each variant's risk allele's frequency with an exact binomial test.

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Cardiovascular Health Study (CHS)

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Diabetes Heart Study (DHS)

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Jackson Heart Study (JHS)

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Family Heart Study (FamHS)

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Lothian Birth Cohort 1936 (LBC1936)

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SHIP / SHIP-Trend

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Genetic Study of Atherosclerosis Risk (GeneSTAR)
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ImaGene
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Old Order Amish
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Framingham Heart Study (FHS)
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Genetic Epidemiology Network of Arteriopathy (GENOA)
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AGES Reykjavik
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Rotterdam Study (RS)
The generation and management of the Illumina exome chip v1.0 array data for the Rotterdam Study (RS-I) was executed by the Human Genotyping Facility of the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. The Exome chip array data set was funded by the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, from the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO)-sponsored Netherlands Consortium for Healthy Aging (NCHA; project nr. 050-060-810); the Netherlands Organization for Scientific Research (NWO; project number 184021007) and by the Rainbow Project (RP10; Netherlands Exome Chip Project) of the Biobanking and Biomolecular Research Infrastructure Netherlands (BBMRI-NL; www.bbmri.nl). We thank Ms. Mila Jhamai, Ms. Sarah Higgins, and Mr. Marijn Verkerk for their help in creating the exome chip database, and Carolina Medina-Gomez, MSc, Lennard Karsten, MSc, and Linda Broer PhD for QC and variant calling. Variants were called using the

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Young Finns Study (YFS)
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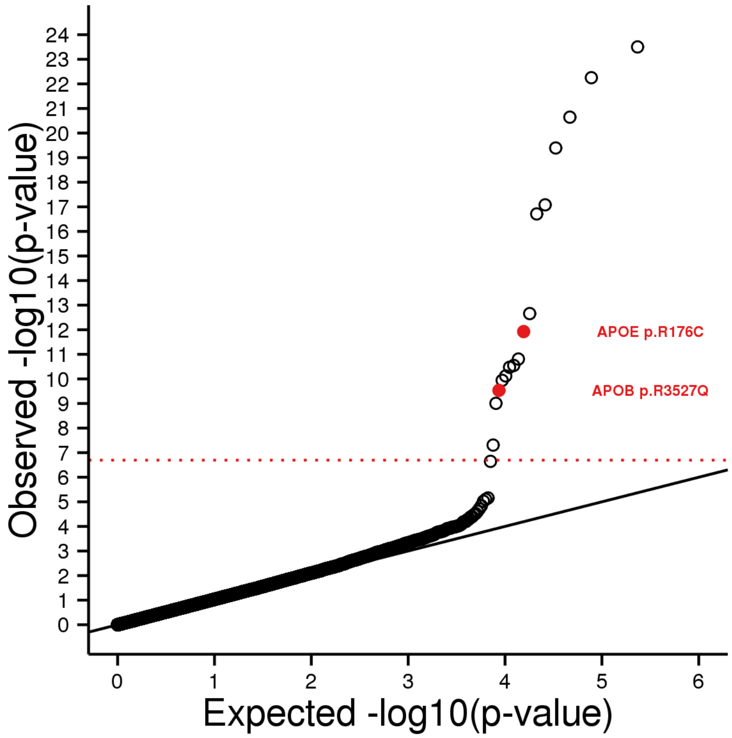
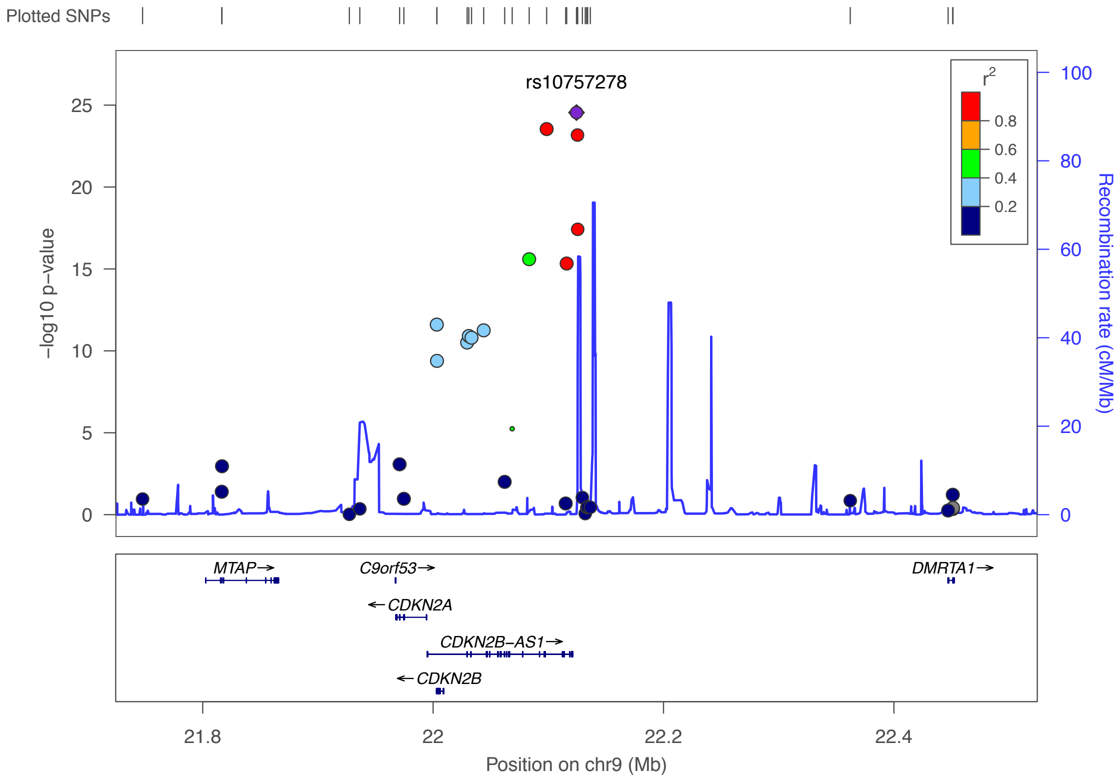
Figure S1. Quantile-quantile plot of coronary artery calcification quantity.



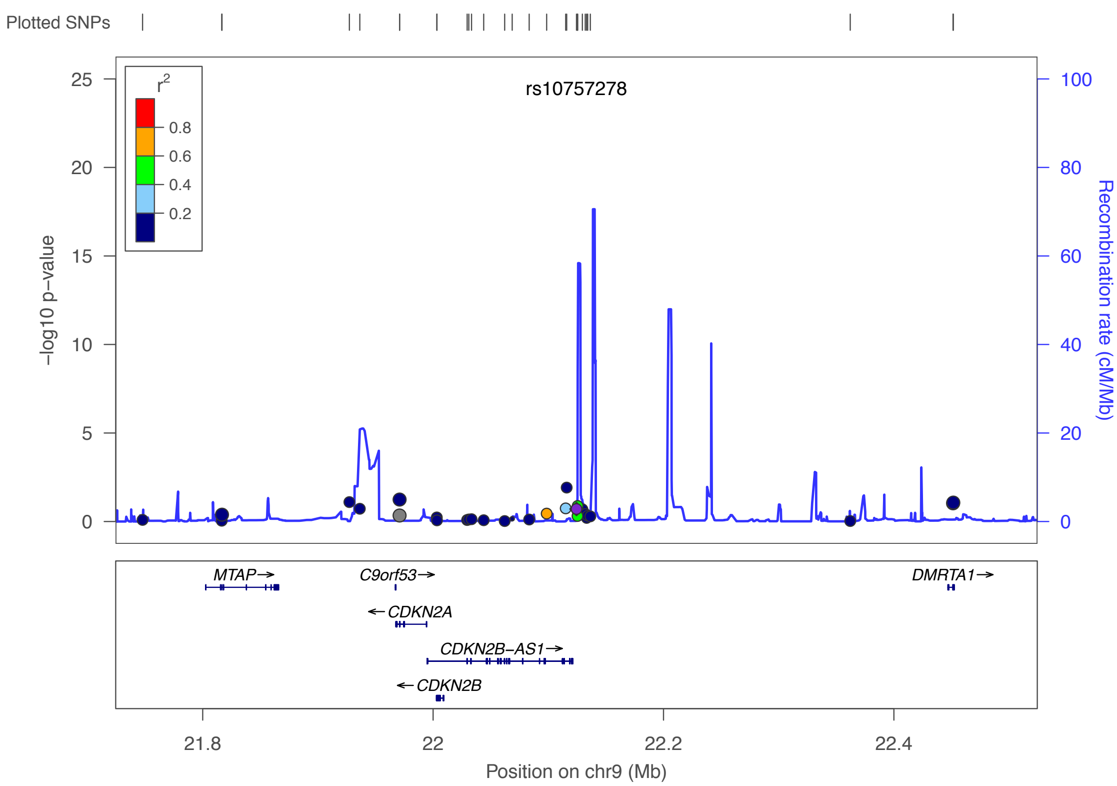
The expected association p-values for the distribution of genotyped versus the observed distribution of p-values for CAC quantity association is displayed. Significant systemic inflation is not observed (λ_{GC} = 1.057). The dotted red line represents the pre-specified threshold for statistical significance accounting for the number of individual variants tested for association (0.05 / 238,065 = 2.10 x 10^{-7}). Lead variants of novel significant associated loci (*APOE* p.R176C and *APOB* p.R3527Q) are highlighted in red.

Figure S2. Regional association plot of coronary artery calcification quantity at 9p21.

A.



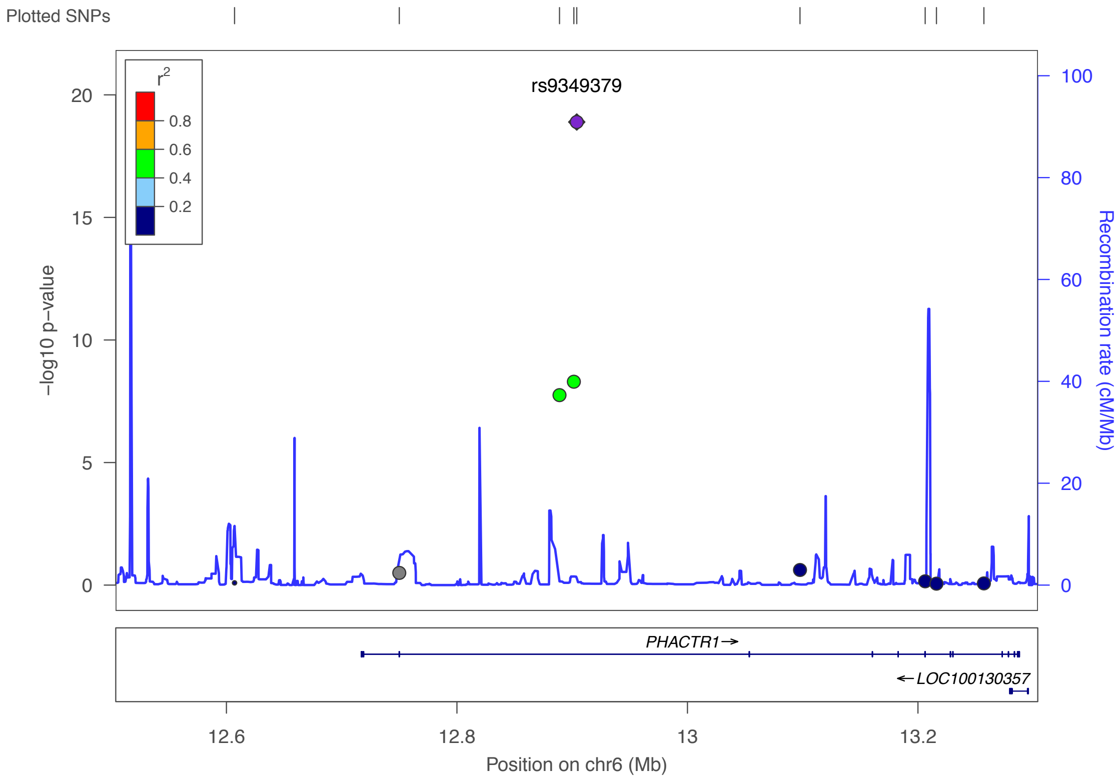
B.



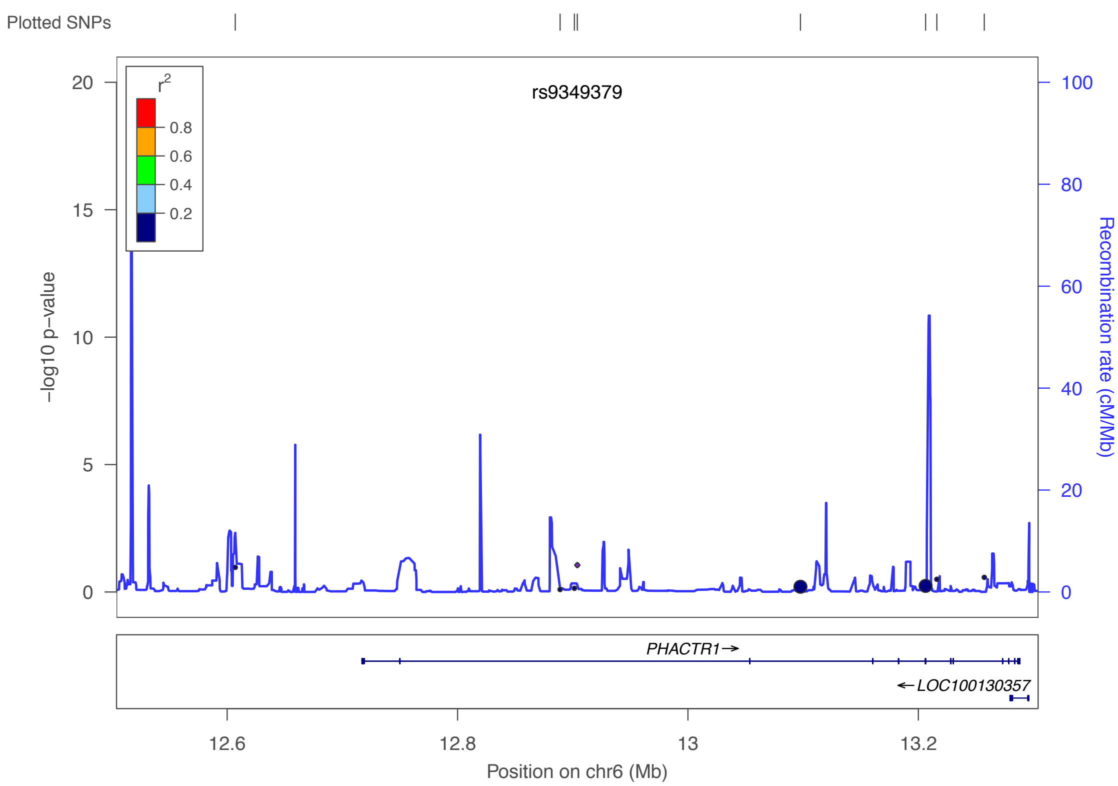
The *CDKN2B* gene resides in the 9p21 genomic region. These regional association plots demonstrate the strength of association, by –log10(p-value), for the lead 9p21 variant, rs10757278, and each genotyped variant within +/- 400 kilobases. Color-coding based on ethnic-specific correlation observed in the 1000 Genomes Project is demonstrated. Dot sizes are scaled to the number genotyped for a given variant. Plots are separately shown for participants of: **A.** European ancestry and **B.** African ancestry.

Figure S3. Regional association plots of coronary artery calcification quantity at 6p24.

A.



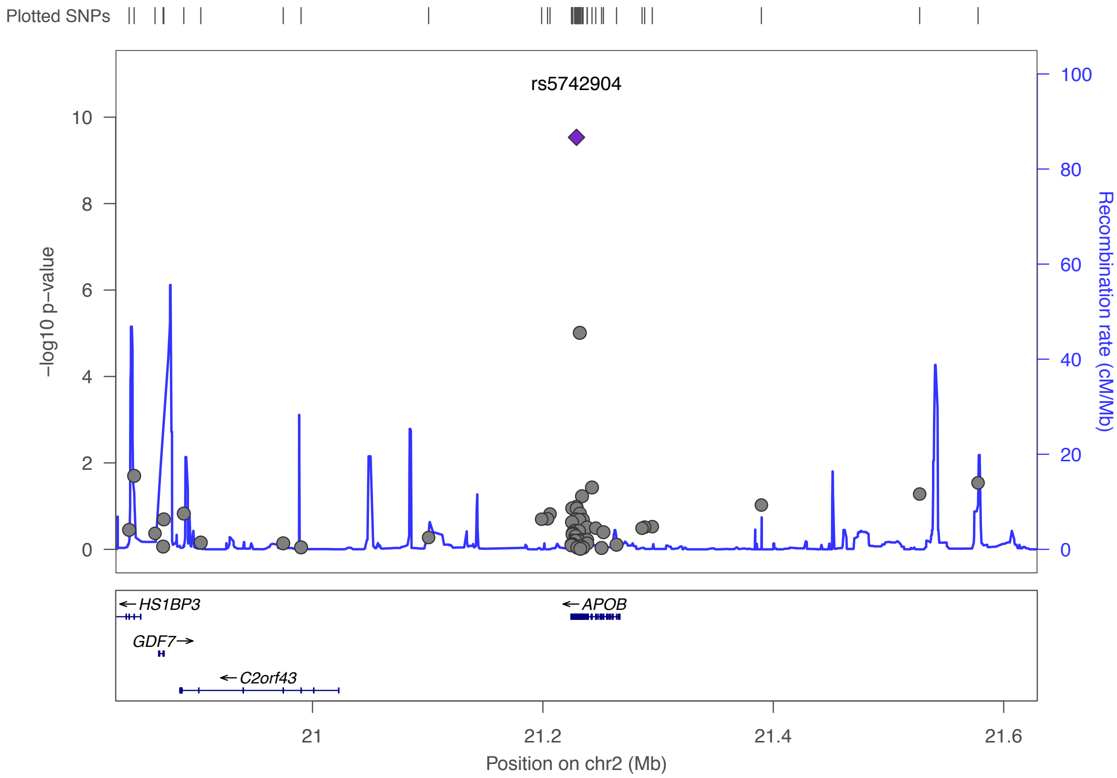
B.



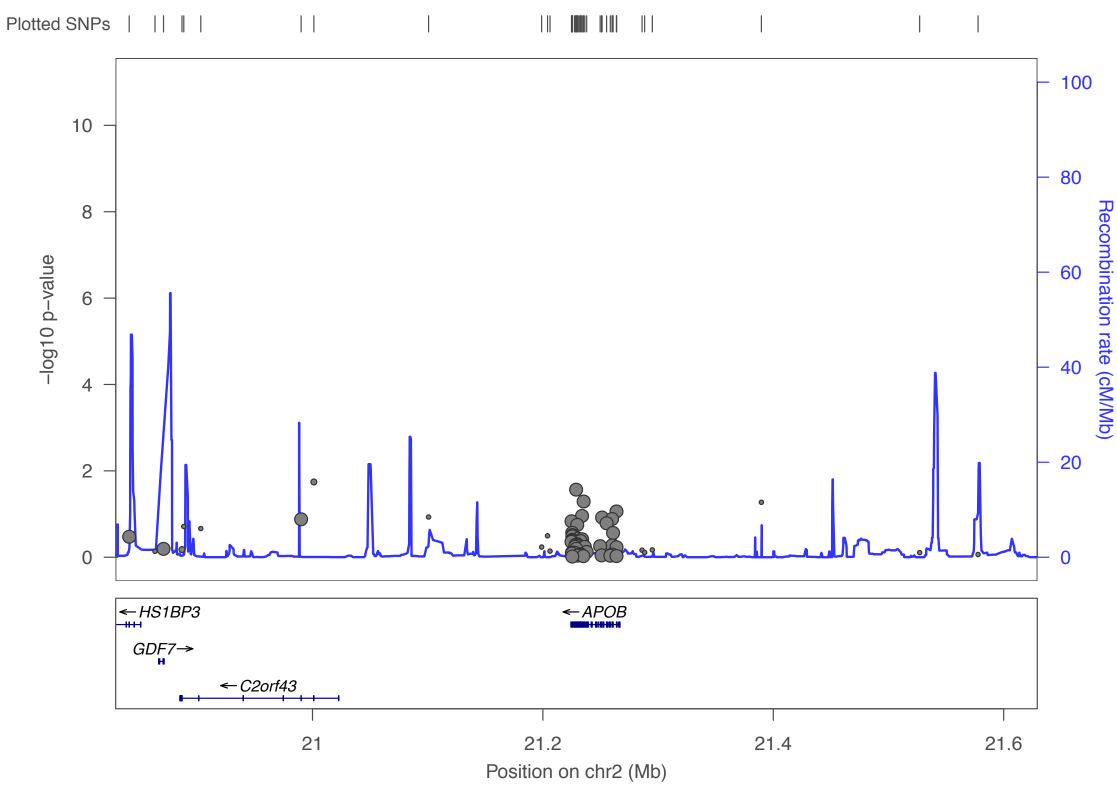
The *PHACTR1* gene resides in the 6p24 genomic region. These regional association plots demonstrate the strength of association, by –log10(p-value), for the lead 6p24 variant, rs9349379, and other genotyped variants within +/- 400 kilobases. Color-coding based on ethnic-specific correlation observed in the 1000 Genomes Project is demonstrated. Dot sizes are scaled to the number genotyped for a given variant. Plots are separately shown for participants of: **A.** European ancestry and **B.** African ancestry.

Figure S4. Regional association plots of coronary artery calcification quantity at 2p24.

A.



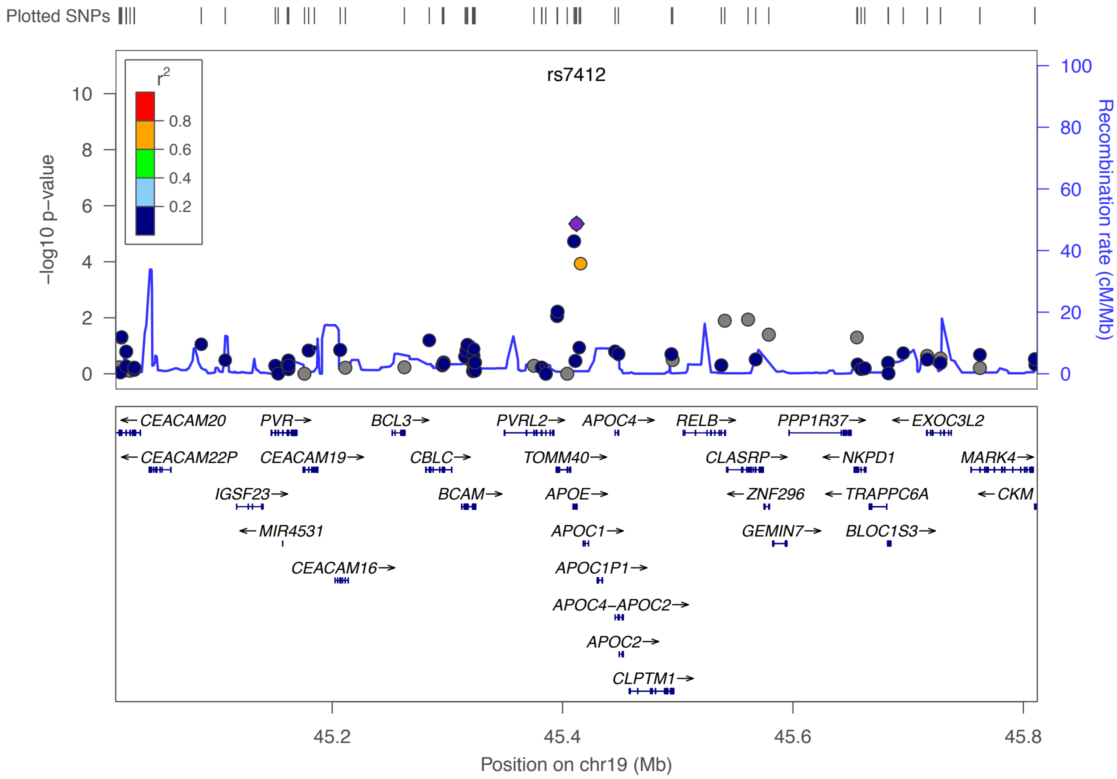
B.



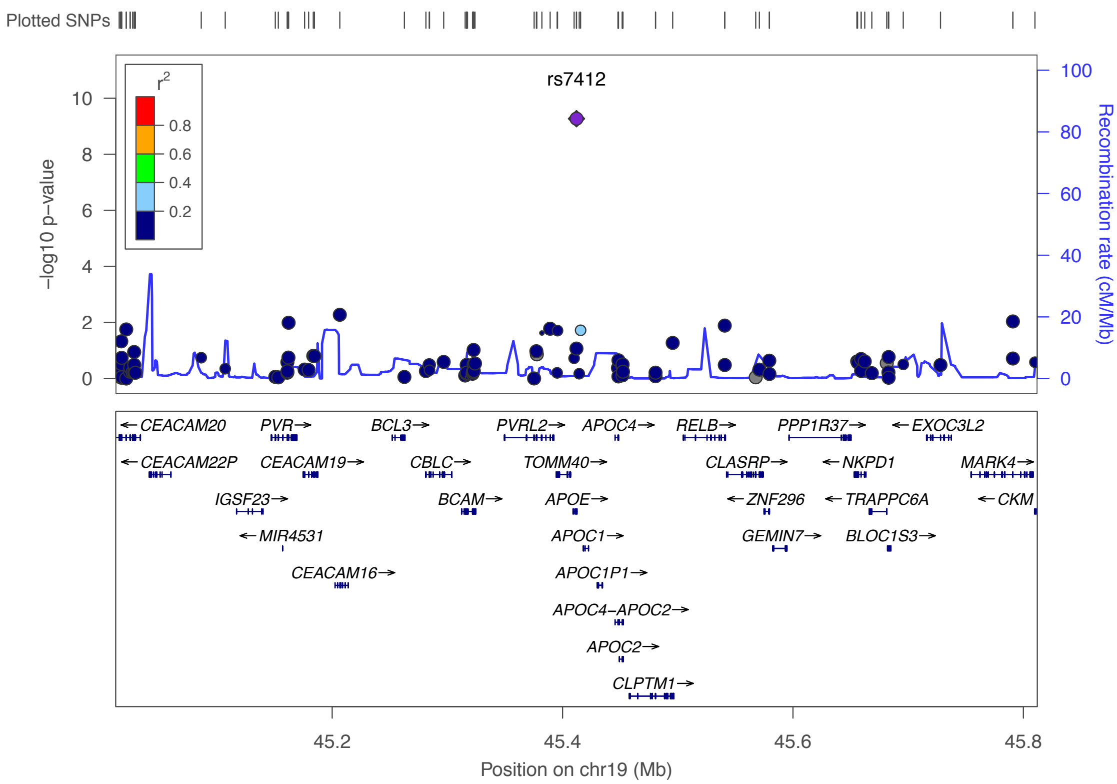
The *APOB* gene resides in the 2p24 genomic region. These regional association plots demonstrate the strength of association, by –log10(p-value), for the lead 2p24 variant, rs5742904, and each genotyped variant within +/- 400 kilobases. Color-coding based on ethnic-specific correlation observed in the 1000 Genomes Project is demonstrated. Dot sizes are scaled to the number genotyped for a given variant. Plots are separately shown for participants of: **A.** European ancestry and **B.** African ancestry.

Figure S5. Regional association plots of coronary artery calcification quantity at 19q13.

A.



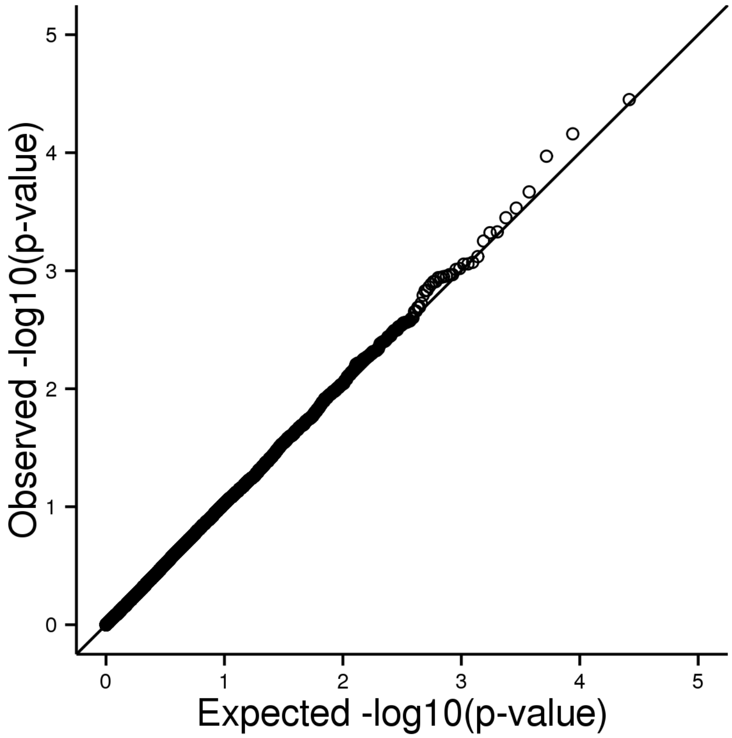
B.



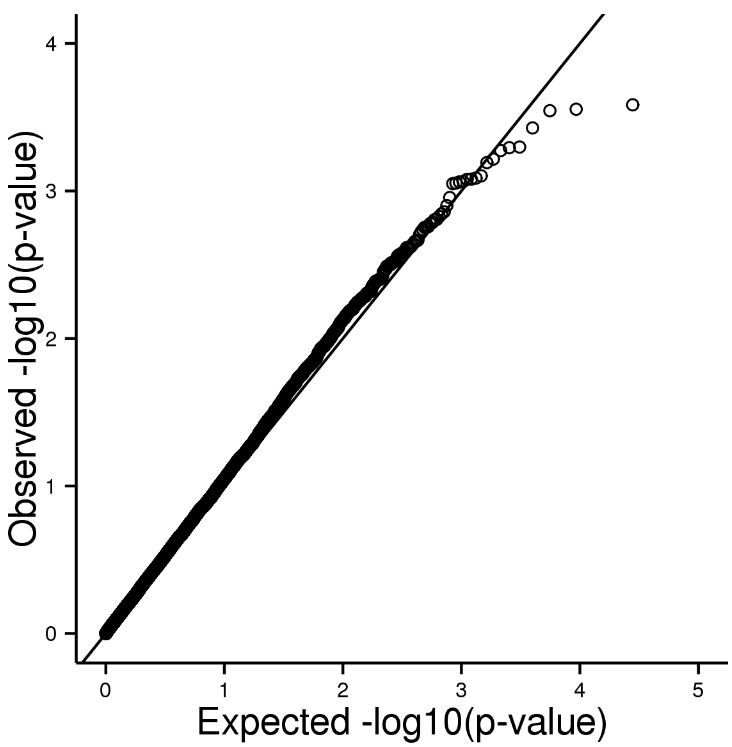
The *APOE* gene resides in the 19q13 genomic region. These regional association plots demonstrate the strength of association, by –log10(p-value), for the lead 19q13 variant, rs7412, and each genotyped variant within +/- 400 kilobases. Color-coding based on ethnic-specific correlation observed in the 1000 Genomes Project is demonstrated. Dot sizes are scaled to the number genotyped for a given variant. Plots are separately shown for participants of: **A.** European ancestry and **B.** African ancestry.

Figure S6. Quantile-quantile plots of coronary artery calcification quantity gene-based association.

A.

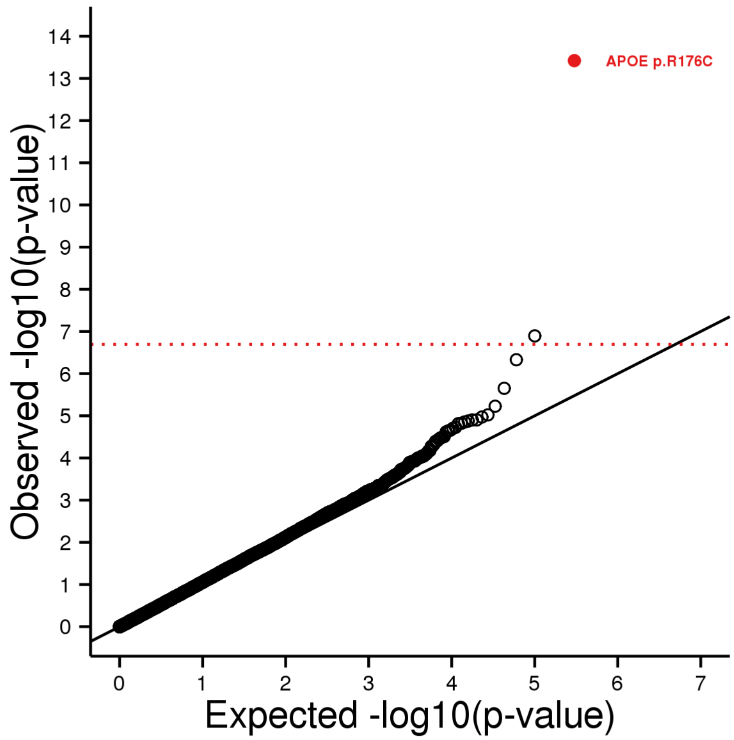


B.



The expected associations p-values for the distribution of genotyped versus the observed distributions of p-values for CAC quantity gene-based association is displayed. Systemic inflation is not observed (T1 λ_{GC} = 1.026, SKAT λ_{GC} = 1.107). Significant observed deviations from the expected distribution are not noted. Association analyses are displayed for: **A.** T1 and **B.** SKAT.

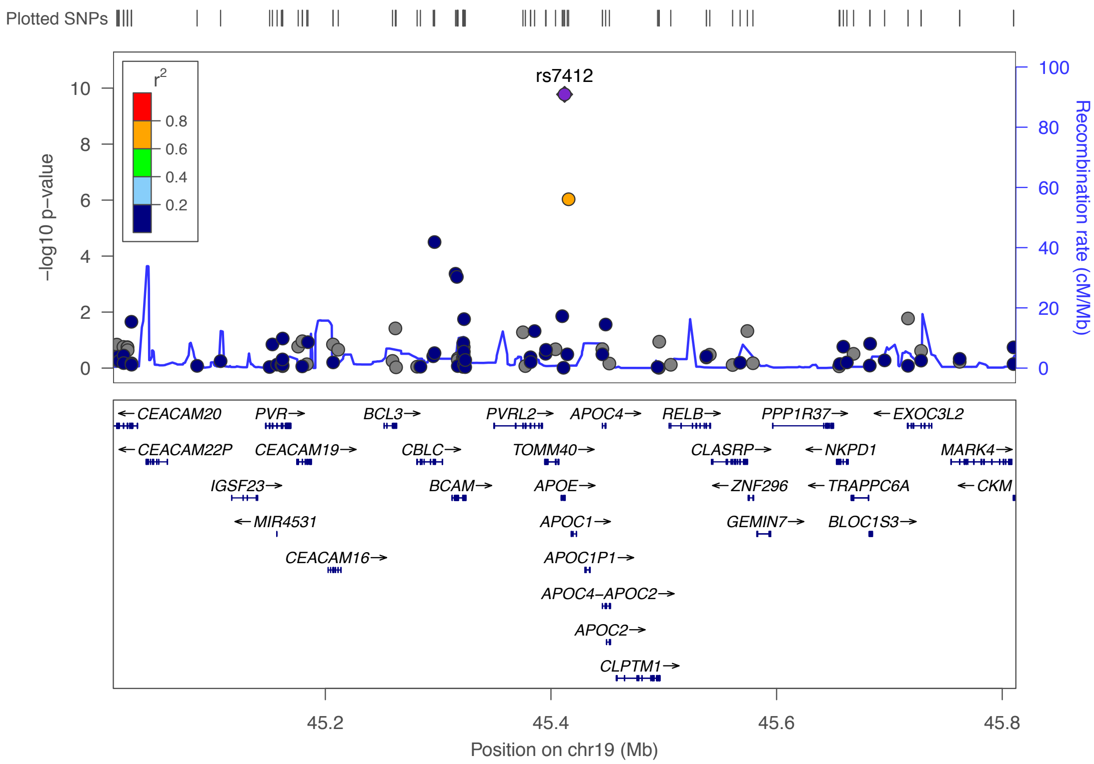
Figure S7. Quantile-quantile plot of carotid intima media thickness single variant association.



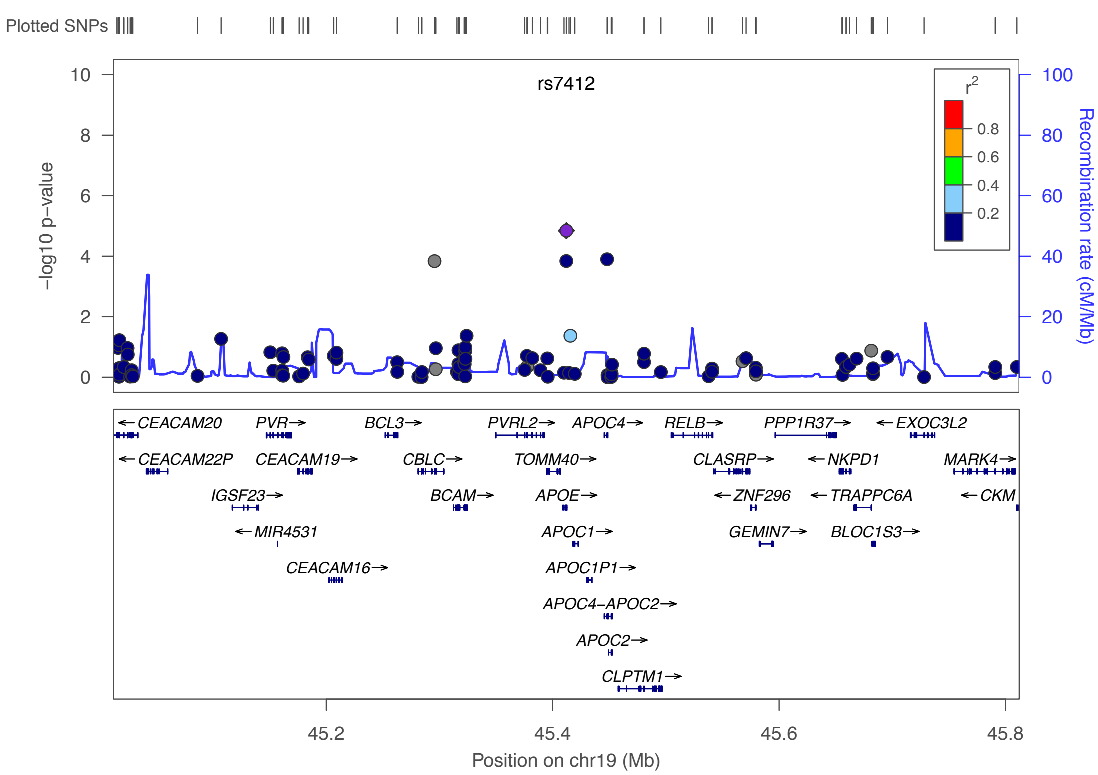
The expected association p-values for the distribution of genotyped versus the observed distribution of p-values for CIMT association is displayed. Systemic inflation is not observed (λ_{GC} = 1.080). The dotted red line represents the prespecified threshold for statistical significance accounting for the number of individual variants tested for association (0.05 / 238,065 = 2.1×10^{-7}). The lead variant of the novel significant associated locus (*APOE* p.R176C) is highlighted in red.

Figure S8. Regional association plots of carotid intima media thickness at 19q13 (*APOE*).

A.



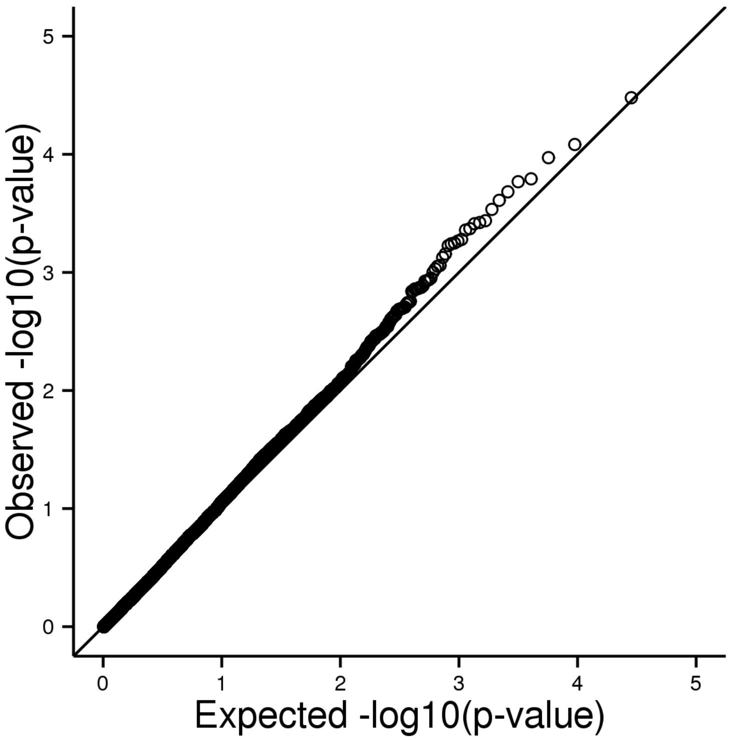
B.



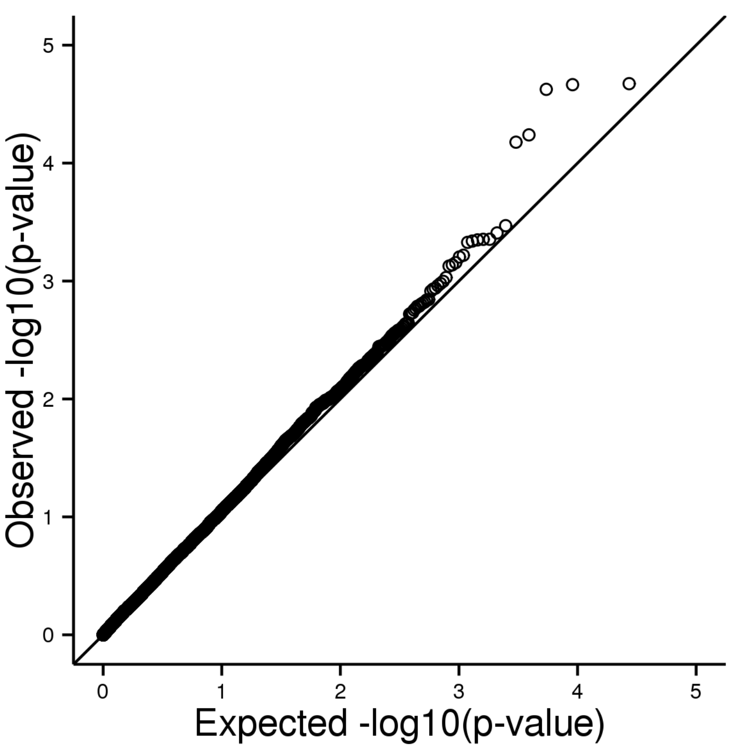
The *APOE* gene resides in the 19q13 genomic region. These regional association plots demonstrate the strength of association, by –log10(p-value), for the lead 19q13 variant, rs7412, and each genotyped variant within +/- 400 kilobases. Color-coding based on ethnic-specific correlation observed in the 1000 Genomes Project is demonstrated. Dot sizes are scaled to the number genotyped for a given variant. Plots are separately shown for participants of: **A.** European ancestry and **B.** African ancestry.

Figure S9. Quantile-quantile plot of carotid intima media thickness gene-based association.

A.

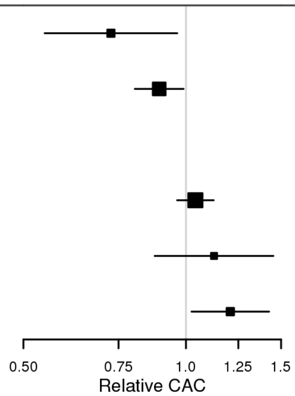


B.



The expected associations p-values for the distribution of genotyped versus the observed distributions of p-values for CIMT gene-based association is displayed. Significant systemic inflation is not observed (T1 $\lambda_{GC} = 1.043$, SKAT $\lambda_{GC} = 1.114$). Significant observed deviations from the expected distribution are not noted. Association analyses are displayed for: **A.** T1 and **B.** SKAT.

Figure S10. Association of major *APOE* genotypes with CAC.



Genotype	Frequency	Relative CAC	95% CI
ε2/ε2	0.01	0.73	(0.55,0.96)
ε2/ε3	0.12	0.89	(0.80,0.99)
ε3/ε3	0.62	1.00	(1.00,1.00)
ε4/ε3	0.21	1.04	(0.96,1.13)
ε4/ε4	0.02	1.13	(0.87,1.45)
ε4/ε2	0.03	1.21	(1.02,1.43)

Major *APOE* genotypes ascertained by PCR were obtained in 5,872 individuals and were associated with log-transformed CAC quantity relative to the ε3/ε3 referent genotype within six cohorts accounting for age, sex, and ethnicity. Effect estimates were combined using fixed-effects meta-analysis and are displayed.

Table S1. Demographics of Participants by Cohort in CAC Analysis

Cohort	Ethnicity	Years measured		N	Age, y mean (sd)	Women, n (%)	CAC Score, median (IQR)	CAC>0, n (%)	CAC>100, n (%)	Hypertension, n (%)	Hypercholesterolemia, n (%)	Diabetes mellitus, n (%)	Recent cigarette smoker, n (%)	Device	References
Cardiovascular Health Study	EA	Baseline	1989-90	339	70.6 (3.8)	210 (62%)	368 (74.15, 826.65)	311 (92%)	237 (70%)	147 (43%)	103 (30%)	27 (8%)	39 (12%)	Imatron C-150	27
	AA	Baseline	1989-90, 1992-93	104	70.9 (4.0)	59 (57%)	124.85 (7.15, 499.02)	88 (85%)	55 (53%)	70 (67%)	20 (19%)	21 (21%)	18 (17%)	Imatron C-150	
Diabetes Heart Study	EA	Baseline	1998-2006	667	60.9 (9.5)	416 (62%)	102.5 (12.0, 673.0)	326 (91%)	208 (58%)	544 (81.56 %)	290 (43.67%)	527 (79%)	110 (17%)	General Electric CT system (CTi, LightSpeed QXi&Pro16 system, GE Medical Systems, Waukesha, WI)	28
Jackson Health Study	AA	Baseline	2005-08	1355	59.4 (10.9)	448 (33%)	0.0 (0.0, 65.62)	619 (46%)	283 (21%)	801 (59%)	233 (17%)	178 (13%)	402 (30%)	Lightspeed 16 Pro (GE Healthcare, Milwaukee, WI)	29
Family Heart Study	EA	Baseline	2002-04	2370	55.6 (13.1)	1388 (59%)	0.5 (0.0, 78.0)	1304 (55%)	540 (23%)	855 (36%)	652 (28%)	258 (11%)	234 (10%)	GE LightSpeed Plus, Siemens Volume Zoom, Philips/Marconi MX 8000	5, 30
	AA	Baseline	2002-04	537	52.4 (10.7)	363 (68%)	0 (0.00,28 .00)	266 (50%)	78 (15%)	385 (72%)	117 (22%)	120 (23%)	118 (22%)	GE LightSpeed Plus	
GeneSTAR	EA	Baseline or Follow up	2001, 2003-07, 2008-12	488	49.4 (10.3)	255 (52%)	0 (0, 29.7)	205 (42%)	78 (16%)	187 (38%)	172 (35%)	42 (9%)	83 (17%)	2001-07: Siemens Volume Zoom MDCT; 2008-12: Siemens SOMATOM	31

	AA	Baseline or Follow up	2001, 2003-07, 2008-12	290	50.0 (10.3)	194 (67%)	0 (0, 2.6)	94 (32%)	25 (9%)	163 (56%)	74 (26%)	49 (17%)	81 (28%)	Definition Flash dual-source 256 MDCT 2001-07: Siemens Volume Zoom multidetector row computed tomograph; 2008-12: Siemens SOMATOM Definition Flash dual-source 256 multi-detector scanner	
NELSON	**AA**	Baseline	2003-06	905	62.0 (6.0)	6 (1%)	97.41 (1.97, 654.47)	706 (78%)	452 (50%)	N/A	N/A	N/A	N/A	Mx8000 IDT, Somatom Sensation 16, Brilliance 16P	32, 33
Old Order Amish	**EA**	Baseline	2001-06	1075	56.6 (13.1)	591 (55%)	2.40 (0, 144.86)	568 (53%)	304 (26%)	198 (18%)	453 (42%)	45 (4%)	84 (8%)	Imatron C-150	8
FHS	**EA**	Follow up	2005	3184	52.2 (11.6)	1543(48 %)	0 (0, 45.26)	1204 (38%)	598 (19%)	905 (28%)	722 (23%)	183 (6%)	413 (13%)	LightSpeed Ultra (GE)	9, 10
BioImage	**EA**	Baseline	2008-09	4182	69.1 (6.0)	2357 (56%)	57.0 (0.0, 274.0)	2983 (71%)	1783 (43%)	2944 (70%)	2713 (65%)	686 (16%)	357 (9%)	Philips Brilliance 64-slice MDCT (Philips Healthcare, Andover, Massachusetts)	11, 34
	AA	Baseline	2008-09	843	67.9 (5.7)	501 (59%)	2.0 (0.0, 77.5)	443 (53%)	179 (21%)	708 (84%)	545 (65%)	250 (30%)	80 (9%)		
MESA	**EA**	Baseline	2000-02	2526	62.7 (10.2)	1320 (52%)	9.35 (0,6452. 61)	1438 (57%)	780 (31%)	975 (39%)	707 (28%)	151(6%)	287 (11%)	Wake Forest: Light Speed Plus, Light Speed QX/I; Columbia, Northwestern, UCLA: Imatron C-150; Johns Hopkins and	30, 35
	AA	Baseline	2000-02	1611	62.3 (10.1)	868 (54%)	0 (0,5599. 43)	721 (45%)	311 (19%)	959(59.53%)	367 (23%)	279 (17%)	194 (13%)		

														Minnesota: Volume Zoom	
GENOA	**EA**	Follow up	2000 - 04	1033	58.0 (10.1)	615 (59%)	10.67 (0.0, 141.86)	680 (66%)	298 (29%)	727 (70%)	370 (36%)	136 (13%)	87 (18%)	Imatron C-150	[29, 36]
	AA	Follow up	2009 - 11	354	67.3 (8.4)	257 (73%)	11.09 (0.0, 196.27)	213 (60%)	114 (32%)	293 (83%)	163 (46%)	120 (34%)	27 (19%)	Lightspeed 16 Pro (GE Healthcare, Milwaukee, WI)	
AGES Reykjavik	**EA**	Baseline	2002-04	2286	76.2 (5.5)	1457 (63.8%)	(22.59,604.76)	1948 (85%)	1377 (60%)	1763 (77%)	NA	236 (10%)	296 (13%)	Siemens Somatom Sensation 4 MDCT (Siemens Medical Solutions, Malvern, PA)	[37]
Rotterdam Study	**EA**	Follow up	1997-99	785	71.8 (5.9)	353 (45%)	146.47 (20.50, 539.09)	734 (94%)	443 (56%)	502 (64%)	311 (40%)	97 (12%)	165 (21%)	C-150 Imatron EBCT (GE-Imatron Inc., South San Francisco, CA)	[38]
Young Finns Study	**EA**	Follow up	2007	499	41.7 (2.6)	284 (57%)	0.00 (0.00, 0.00)	96 (19%)	13 (3%)	136 (27%)	76 (15%)	7 (1%)	83 (17%)	GE Discovery VCT 64-slice CT/PET (GE Healthcare, Milwaukee, WI) (Turku), Philips Brilliance 64-slice CT (Philips Medical Systems, Best, Netherlands) (Tampere), Siemens Somatom Sensation 16-	[39]

	slice CT (Siemens Healthcare, Erlangen, Germany) (Kuopio)

Table S2. Demographics of Participants by Cohort in CIMT Analysis

Cohort	Ethnicity	Years measured		N	Age, y mean(sd)	Women, n (%)	CIMT, mm median (IQR)	Carotid plaque, n (%)	Hypertension, n (%)	Hypercholesterolemia, n (%)	Diabetes mellitus, n (%)	Recent cigarette smoker, n (%)	Device	References
Cardiovascular Health Study	**EA**	Baseline	1989-90	4040	72.8(5.6)	2276 (56%)	1.015 (0.91, 1.14)	2722 (70%)	2234 (55%)	1033 (26%)	557 (14%)	426 (11%)	B-mode US (model SSA-270A; Toshiba)	40
	AA	Baseline	1989-90, 1992-93	738	72.8(5.7)	461 (62%)	1.09 (0.97, 1.22)	552 (75%)	536 (73%)	174 (24%)	166 (23%)	122 (17%)		
Diabetes Heart Study	**EA**	Baseline	1998-2006	647	60.5(9.7)	413 (64%)	0.631 (0.567, 0.706)	NA	527 (81%)	272 (42%)	510 (79%)	113 (18%)	B-mode US (model AU5; Biosound Esaote)	41
Jackson Heart Study	**AA**	Baseline	2000-04	1979	60.0(10.5)	678 (34%)	0.70 (0.60, 0.82)	NA	1209 (61%)	348 (18%)	285 (14%)	621 (31%)	B-mode US (Hewlett Packard Sonos 4500)	42
Lothian Birth Cohort 1936	**EA**	Follow up	2007-10	746	72.8(0.8)	346 (48%)	0.85 (0.70, 0.95)	NA	NA	NA	NA	NA	B-mode US	6
SHIP	**EA**	Baseline	1997-2001	3504	52.8(13.5)	1742 (50%)	0.81 (0.24)	1864 (53%)	1891 (54%)	NA	403 (12%)	985 (28%)	B-Mode US (Diasonics VST Gateway, Santa Clara, California, USA)	7, 43
SHIP-Trend	**EA**	Baseline	2008-12	3461	52.1(15.3)	1770 (51%)	0.72 (0.24)	1425 (41%)	1646 (48%)	NA	433 (13%)	868 (25%)	B-Mode US (vivid-i, GE Medical Systems, Waukesha, Wisconsin, WI, USA)	7, 43
GeneSTAR	**EA**	Follow	2009-12	441	50.0(11.3)	236	0.679	NA	147 (33%)	148 (34%)	37 (8%)	74 (17%)	B-mode US	31, 44

		up				(54%)	(0.504, 0.854)						(model Philips CX50)	
	AA	Follow up	2009-12	251	49.9(11.8)	158 (63%)	0.721 (0.547, 0.895)	NA	130 (52%)	82 (33%)	43 (17%)	69 (27%)		
FHS	**EA**	Baseline	1995-99	3030	58.5(9.7)	1614 (53%)	0.70 (0.63, 0.80)	534 (18%)	1218 (40%)	869 (29%)	297 (10%)	473 (16%)	Toshiba SSH-140A imaging unit with a 7.0 MHz transducer	9, 10
BioImage	**EA**	Baseline	2008-09	4378	69.1(6.0)	2449 (56%)	0.73 (0.65, 0.84)	3487 (80%)	3098 (71%)	2845 (65%)	722 (17%)	380 (9%)	Philips iU22 US systems (Philips Healthcare, Bothell, Washington)	11, 34
	AA	Baseline	2008-09	885	68.0(5.7)	528 (60%)	0.75 (0.68, 0.87)	572 (65%)	748 (85%)	566 (64%)	269 (30%)	85 (10%)	Philips iU22 US systems (Philips Healthcare, Bothell, Washington)	
MESA	**EA**	Baseline	2000-02	2501	62.6(10.3)	1307 (53%)	0.84 (0.47,2.45)	NA	963 (39%)	698(28%)	150 (6%)	282 (11%)	B-mode US (Logiq 700 ultrasound device (GE Med Systems, Waukesha, WI))	45, 46
	AA	Baseline	2000-02	1573	62.2(10.3)	848 (54%)	0.89(0.40,2.39)	NA	928 (59%)	357(23%)	273 (17%)	291 (19%)		
AGES Reykjavik	**EA**	Baseline	2002-04	2835	73.6(5.5)	1629 (58%)	1.13 (1.02,1.24)	NA	2288 (81%)	NA	329 (12%)	357 (13%)	B-Mode US	37
ARIC	**EA**	Baseline	1987-89	8668	54.3(5.7)	4594 (47%)	0.76 (0.65, 0.85)	1628 (19%)	2301 (27%)	2216 (26%)	723 (8%)	2155 (25%)	B-mode US	15
	AA	Baseline	1987-89	2662	53.9(5.9)	1647 (62%)	0.78 (0.69, 0.90)	457 (17%)	1493 (56%)	685 (27%)	531 (20%)	851 (32%)		
Rotterdam Study	**EA**	Baseline	1990-93	2500	69.5(8.4)	1341 (54%)	0.99 (0.88,	1451 (58%)	1332 (53%)	1493 (60%)	252 (10%)	607 (24%)	7.5 MHz linear array	47

							1.12)						transducer (ATL UltraMark IV; Advanced Technology Laboratories, Bethel, Washington)	
ERF	**EA**	Baseline	2002-05	1050	49.8(14.2)	564 (54%)	0.78 (0.68, 0.94)	624 (59%)	550 (52%)	364 (35%)	72 (7%)	398 (38%)	7.5 MHz linear-array transducer (ATL 77 UltraMark IV; Advanced Technology Laboratories, Bethel, Washington)	48
NEO	**EA**	Baseline	2008-12	5666	56.0(5.9)	2943 (52%)	0.99 (0.89, 1.10)	NA	1820 (32%)	1669 (30%)	572 (10%)	896 (16%)	7.5-10 MHz linear-array transducer (Art.Lab v2.1, Esaote, Maastricht, The Netherlands)	19
Young Finns Study	**EA**	Follow up	2001, 2007	1974	37.3(5.3)	1100 (56%)	0.61 (0.56,0.67)	54 (3%)	350 (18%)	234 (12%)	23 (1%)	352 (18%)	13.0 MHz linear-array transducer, Sequoia 512 ultrasound mainframes (Acuson Inc., Mountain View, CA)	49

Table S3. ***APOE*** **ε2 association with CAC adjusted for blood lipids.**

	All N = 20,527			**EA N = 15,398**			**AA N = 5,129**		
Adjustment	**Beta**	**SE**	***P***	**Beta**	**SE**	***P***	**Beta**	**SE**	***P***
Base Model	-0.2519	0.0373	1.54×10^{-11}	-0.1792	0.0442	4.94×10^{-5}	-0.4346	0.0700	5.36×10^{-10}
LDL cholesterol	-0.1862	0.0332	2.08×10^{-8}	-0.1748	0.0455	1.23×10^{-4}	-0.1993	0.0486	4.14×10^{-5}
HDL cholesterol	-0.2061	0.0327	2.95×10^{-10}	-0.1701	0.0447	1.44×10^{-4}	-0.2473	0.0479	2.45×10^{-7}
Triglycerides	-0.2260	0.0326	4.45×10^{-12}	-0.1942	0.0448	1.44×10^{-5}	-0.2619	0.0477	3.95×10^{-8}
Total cholesterol	-0.1851	0.0329	1.78×10^{-8}	-0.1630	0.0450	2.91×10^{-4}	-0.2103	0.0481	1.26×10^{-5}

For individuals where fasting lipids were available, the association of ε2 with CAC was repeated individually adjusting for each of the major blood lipid measures within each cohort and meta-analyzed in a fixed effects model. β-Coefficients are estimated for natural log transformation of total Agatston CAC score+1. The base model was adjusted for age, sex, and principal components of ancestry.

AA = African ancestry; CAC = coronary artery calcification; EA = European ancestry; HDL = high density lipoprotein; LDL = low-density lipoprotein; SE = standard error

Table S4. CHD-associated variants and association with subclinical atherosclerosis

								CAC			CIMT		
Chr	**Pos**	**Gene**	**SNP**	**Effect Allele**	**Effect Allele Frequency**	**OR**	**P**	**Beta**	**SE**	**P**	**Beta**	**SE**	**P**
1	55496039	*PCSK9*	rs11206510	T	0.85	1.08	2.34E-08	-0.0094	0.0273	7.31E-01	-0.0006	0.0014	6.95E-01
1	56965664	*PPAP2B*	rs9970807	C	0.92	1.13	5.00E-14	0.0700	0.0353	4.75E-02	0.0033	0.0019	8.09E-02
1	109818530	*SORT1*	rs646776	T	0.75	1.11	9.01E-19	0.0629	0.0250	1.18E-02	0.0030	0.0013	1.84E-02
1	154422067	*IL6R*	rs4845625	T	0.45	1.05	3.93E-08	0.0655	0.0212	1.97E-03	-0.0006	0.0011	5.83E-01
1	222823529	*MIA3*	rs17465637	C	0.66	1.08	3.52E-12	0.0732	0.0233	1.67E-03	0.0002	0.0012	8.65E-01
2	19942473	*AK097927*	rs16986953	A	0.11	1.09	1.45E-08	0.1468	0.0423	5.15E-04	-0.0009	0.0021	6.60E-01
2	21286057	*APOB*	rs515135	C	0.79	1.07	3.09E-08	0.0272	0.0276	3.24E-01	0.0038	0.0014	9.12E-03
2	44073881	*ABCG5-ABCG8*	rs6544713	T	0.32	1.05	8.88E-07	0.0240	0.0227	2.90E-01	0.0010	0.0012	3.91E-01
2	85809989	*VAMP5-VAMP8-GGCX*	rs1561198	T	0.46	1.06	6.37E-10	0.0433	0.0208	3.78E-02	0.0005	0.0011	6.16E-01
2	145801461	*ZEB2-ACO74093.1*	rs2252641	C	0.48	1.03	5.16E-04	0.0317	0.0210	1.32E-01	0.0001	0.0011	9.35E-01
3	138122122	*MRAS*	rs9818870	T	0.14	1.07	2.21E-06	0.0338	0.0293	2.48E-01	0.0002	0.0015	8.76E-01
4	156635309	*GUCY1A3*	rs7692387	G	0.81	1.07	7.35E-09	0.0113	0.0265	6.70E-01	0.0014	0.0014	3.08E-01
6	12903957	*PHACTR1*	rs9349379	G	0.43	1.14	1.81E-42	0.1922	0.0212	1.28E-19	-0.0006	0.0011	6.00E-01
6	39174922	*KCNK5*	rs10947789	T	0.78	1.05	1.63E-06	-0.0126	0.0242	6.04E-01	-0.0004	0.0013	7.25E-01
6	160863532	*SLC22A3-LPAL2-LPA*	rs2048327	C	0.35	1.06	2.46E-09	-0.0041	0.0219	8.52E-01	-0.0014	0.0011	2.20E-01
6	161143608	*PLG*	rs4252120	T	0.74	1.03	3.32E-03	-0.0080	0.0230	7.29E-01	-0.0014	0.0012	2.28E-01
7	19036775	*HDAC9*	rs2023938	C	0.1	1.06	1.36E-04	0.0948	0.0349	6.58E-03	0.0044	0.0018	1.44E-02
7	107244545	*7q22*	rs10953541	C	0.78	1.05	1.02E-05	-0.0207	0.0243	3.95E-01	-0.0002	0.0013	8.96E-01
7	129663496	*ZC3HC1*	rs11556924	C	0.69	1.08	5.34E-11	0.0377	0.0216	8.17E-02	0.0004	0.0011	7.39E-01
8	19813180	*LPL*	rs264	G	0.85	1.06	1.06E-05	0.0536	0.0300	7.46E-02	0.0024	0.0015	1.13E-01
8	126490972	*TRIB1*	rs2954029	A	0.55	1.04	2.61E-06	0.0011	0.0218	9.60E-01	0.0018	0.0012	1.32E-01
9	22098574	*9p21*	rs4977574	G	0.49	1.21	6.35E-98	0.2111	0.0208	2.88E-24	0.0006	0.0011	5.60E-01
9	136154168	*ABO*	rs579459	C	0.21	1.08	1.14E-10	0.0450	0.0262	8.62E-02	-0.0030	0.0014	2.81E-02

10	30335122	*KIAA1462*	rs2505083	C	0.40	1.06	1.57E-10	0.0732	0.0211	5.29E-04	0.0033	0.0011	2.43E-03
10	44753867	*CXCL12*	rs501120	T	0.81	1.08	1.39E-11	0.0672	0.0312	3.13E-02	-0.0032	0.0016	4.91E-02
10	90989109	*LIPA*	rs11203042	T	0.45	1.04	1.22E-04	0.0136	0.0210	5.16E-01	-0.0012	0.0011	2.56E-01
10	104719096	*CYP17A1-CNNM2-NT5C2*	rs12413409	G	0.89	1.08	1.07E-07	-0.0296	0.0377	4.31E-01	0.0014	0.0019	4.50E-01
11	103660567	*PDGFD*	rs974819	T	0.33	1.07	2.44E-10	0.0818	0.0233	4.56E-04	0.0033	0.0012	7.15E-03
11	116648917	*ZNF259-APOA5-APOA1*	rs964184	G	0.19	1.05	5.60E-05	0.0288	0.0295	3.30E-01	-0.0010	0.0017	5.45E-01
12	90008959	*ATP2B1*	rs2681472	G	0.20	1.08	6.17E-11	0.0956	0.0279	6.17E-04	-0.0053	0.0015	2.78E-04
12	111884608	*SH2B3*	rs3184504	T	0.42	1.07	1.03E-09	-0.0062	0.0208	7.67E-01	-0.0015	0.0011	1.50E-01
13	28973621	*FLT1*	rs9319428	A	0.31	1.04	7.13E-05	0.0081	0.0224	7.17E-01	-0.0029	0.0012	1.38E-02
14	100133942	*HHIPL1*	rs2895811	C	0.41	1.04	1.86E-05	0.0283	0.0212	1.81E-01	0.0004	0.0011	6.93E-01
15	91416550	*FURIN-FES*	rs17514846	A	0.44	1.05	3.10E-07	-0.0410	0.0210	5.08E-02	0.0019	0.0011	8.59E-02
17	2126504	*SMG6*	rs216172	C	0.35	1.05	5.07E-07	0.0461	0.0217	3.36E-02	-0.0031	0.0012	1.05E-02
17	17543722	*RAI1-PEMT-RASD1*	rs12936587	G	0.61	1.03	8.24E-04	0.0153	0.0219	4.86E-01	0.0014	0.0011	2.11E-01
17	46988597	*UBE2Z*	rs46522	T	0.51	1.04	1.84E-05	0.0434	0.0208	3.71E-02	0.0001	0.0011	9.27E-01
19	11163601	*LDLR*	rs1122608	G	0.77	1.08	2.73E-11	0.0188	0.0243	4.39E-01	0.0036	0.0013	7.59E-03
19	45395619	*APOE-APOC1*	rs2075650	G	0.13	1.07	1.61E-06	0.0822	0.0299	6.06E-03	0.0018	0.0015	2.23E-01
21	35599128	*KCNE2* (gene desert)	rs9982601	T	0.13	1.12	1.33E-13	0.0763	0.0324	1.84E-02	-0.0003	0.0016	8.71E-01

Variants that have been previously associated with CHD in individuals of European, South Asian, or East Asian ancestry[26], effect estimates, and risk allele frequencies are displayed. The CAC and CIMT effects estimates and significance for each CHD risk variant among those of European ancestry are also displayed. β-Coefficients for CAC and CIMT are estimated for natural log transformation of total Agatston CAC score+1 and natural log transformation of CIMT, respectively.

CAC = coronary artery calcification; CHD = coronary heart disease; Chr = chromosome; CIMT = carotid intima media thickness; OR = odds ratio; P = p-value; Pos = genomic position (hg19 build); SE = standard error; SNP = single nucleotide polymorphism

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